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Severe Tumor Lysis Syndrome Following Splenic Irradiation

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A 72-year-old man suffering from non-Hodgkin's lymphoma is described. After failing to respond to chlorambucil–prednisone regimen for three months, he was treated by splenic irradiation (total dose 500 cGY) in 10 consecutive daily doses. Two days after the last irradiation, the patient developed acute tumor lysis syndrome (TLS) with extreme blood levels of uric acid (33.7 mg/dl), phosphorus (13.7 mg/dl), potassium (6.08 mEq/l), and calcium (6.8 mg/dl). It should be remembered that the acute TLS, which usually occurs following chemotherapy, can also be radiation-induced. Am. J. Hematol. 60:75–76, 1999. © 1999 Wiley-Liss, Inc.

Key words: tumor lysis syndrome; radiation therapy; acute renal failure; splenic irradiation

INTRODUCTION

The acute tumor lysis syndrome (TLS) is a potentially fatal complication caused by the rapid lysis of a large number of neoplastic cells. This complication usually occurs following effective cytotoxic treatment for rapidly growing cancers, especially acute leukemias and high-grade lymphomas. It is characterized by severe hyperuricemia, hyperphosphatemia, hypocalcemia, and acute renal failure as a consequence of deposition of uric acid crystals and calcium phosphate complexes in the renal tissue. Fatal hyperkalemia and volume overload may develop. Preexisting azotemia and hyperuricemia are important predisposing factors in many patients.

We describe here a patient with non-Hodgkin's lymphoma who developed severe TLS with fatal outcome following splenic irradiation.

CASE REPORT

A 72-year-old man was evaluated for easy bruisability, thrombocytopenia, and splenomegaly. He had a long history of hypertensive cardiovascular disease, ischemic coronary heart disease, chronic bronchitis, and aneurysm of the descending aorta of 4.5 cm in diameter. In the past he underwent a coronary angioplasty and suffered of mild chronic renal failure.

A few months ago a pruritic maculopapular rash developed four weeks after initiation of allopurinol treatment for asymptomatic hyperuricemia. The rash disappeared a few days after medication was discontinued and the serum uric acid concentration remained stable between 8.0–8.5 mg/dl with a purin-restricted diet.

On physical examination, the patient presented with mild dyspnea and peripheral cyanosis. Blood pressure was 160/95 mmHg, the pulse was 80/min regular and his heart sounds were normal. Scattered rales were audible on both lung fields. The spleen was palpable 12 cm below the costal margin, liver span was 10 cm, and lymph nodes were not palpable.

Laboratory tests showed the following: Hemoglobin (Hb), 9.2 g/dl: reticulocyte count of 2.8%; white blood cells, 4.1×10^9/l with a normal differential count. Platelet count was 40×10^9/l; creatinine, 1.7 mg/dl; and uric acid, 8.3 mg/dl. Lactic dehydrogenase was 956 μmol/l (normal range 200–460 μmol/l). Bilirubin, alanine aminotransferase, aspartate aminotransferase, albumin, and alkaline phosphatase were within the normal range. A di-

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rect Coombs' test was positive and haptoglobin was 199 mg/dl (normal range 100–200 mg/dl).

A bone marrow biopsy was diagnosed as non-Hodgkin's lymphoma, with infiltration by small cleaved B lymphocytes.

The patient did not respond to a three-month regimen of chlorambucil and prednisone. The chemotherapy was discontinued and one month later he had an episode of gastrointestinal bleeding. On admission Hb was 6.9 g/dl, white blood cells were 1.4×10^9/l, and platelet count was 6×10^9/l. He was given packed blood cells, platelet transfusions, and high-dose immunoglobulins.

The gastrointestinal bleeding subsided but the pancytopenia persisted and platelet count was remarkably low. Therefore, splenic irradiation of 10 consecutive daily doses of ×50 cGy was initiated.

Blood biochemical parameters prior to initiation of the radiation therapy were as follows: creatinine, 1.8 mg/dl; urea nitrogen, 49 mg/dl; uric acid, 11.5 mg/dl; potassium, 4.3 mEq/l; sodium, 145 mEq/l; calcium, 10.1 mg/dl; phosphorus, 3.2 mg/dl; and lactic dehydrogenase, 648 μmol/l.

Two days after the last irradiation, the patient was readmitted for fever, general deterioration, and anuria. Physical examination on admission revealed a diffuse nonpalpable purpuric rash.

The laboratory tests showed the following: Hb, 6.4 g/dl; white blood cells, 0.89×10^9/l; platelets count, 6×10^9/l; creatinine, 3.4 mg/dl; urea nitrogen, 130 mg/dl; uric acid, 33.7 mg/dl; calcium, 6.8 mg/dl; phosphorus, 13.7 mg/dl; potassium, 6.09 mEq/l; and lactic dehydrogenase, 2,231 μmol/l.

While preparing him for hemodialysis, he developed severe gastrointestinal hemorrhage that did not respond to fluid and blood resuscitation.

DISCUSSION

In almost all the textbooks and review articles, TLS is defined as a number of metabolic abnormalities that occur in patients with lymphoproliferative or solid malignancies following spontaneous or chemotherapy-induced cytolysis. However, the first two reports in the medical literature described patients with radiation-induced TLS. In 1929, Bedrna and Polcak [1] reported occurrence of acute renal failure following x-ray therapy in patients with chronic leukemia. In 1940, Merrill [2] described patients with acute leukemia who developed uremia and hyperuricemia following x-ray therapy.

A survey of the literature disclosed three other, more recent, communications. In 1984, Tomlinson and Solberg [3] described a patient with metastatic medulloblastoma who developed tumor lysis syndrome following paliative radiotherapy for a rapidly expanding abdominopelvic mass.

In 1991, Fleming et al. [4] described radiation-induced TLS in the bone marrow transplant setting and in 1994, Nomdedeu et al. [5] reported acute TLS appearing during chemoradiotherapeutic conditioning for allogeneic bone marrow transplantation in a patient with chronic lymphocytic leukemia.

In conclusion, our case emphasizes the importance of recognizing that the acute TLS may occur following radiation therapy. Adequate pretreatment measures such as allopurinol treatment and vigorous hydration can prevent or attenuate the severity of the TLS in these patients [6–9].

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